

vs 70%, $p = 0.02$), systolic hypertension (53% vs 42%, $p = 0.03$), diabetes (17% vs 8%, $p = 0.002$), no regular exercise (79% vs 60%, $p < 0.001$) and triglycerides (187 ± 77 vs 158 ± 69 mg/dl, $p < 0.001$). The relative risk (RR) of progression was similar for both genders.

Gender	Progression (%)		P value RR (95% CI)	
	AL	ML		
Women	14.8	23.8	0.25	0.55 (0.20-1.50)
Men	28.6	40.1	< 0.001	0.60 (0.47-0.73)

Conclusion: The higher prevalence of associated risk factors in women did not diminish the beneficial effect of aggressive cholesterol lowering in delaying saphenous vein graft atherosclerosis.

1116-3 Evolution of Thoracic Aorta Atherosclerosis in Patients With Heterozygous Familial Hypercholesterolemia After Statin Therapy

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Background: Heterozygous familial hypercholesterolemia (hFH) is associated with an increased risk of atherosclerosis. The aim of this study was to determine the evolution of descending thoracic aorta atheromatous disease (TAA) by transthoracic echocardiography (TEE) in hFH patients after long-term hypolipidemic therapy with diet and statins. Sixteen patients (7 males and 9 females, mean age 47 ± 12 yrs) with newly diagnosed hFH comprised the study population. All patients underwent a baseline TEE examination, after which AHA step I diet and pravastatin (20-40 mg o.d) were initiated. Repeat TEE was performed after 2 yrs of therapy. TAA was graded as follows: grade 0: normal intima; grade I: increased intimal echodensity without thickening or lumen irregularity; grade II: increased intimal echodensity with single well-defined atheromatous plaque protruding <3 mm into the lumen; grade III: multiple atheromas protruding <3 mm; grade IV: atheromas protruding >3 mm; grade V: protruding mobile or pedunculated plaques.

Results: As a result of treatment, LDL decreased from 294 ± 56 mg/dl to 193 ± 56 mg/dl ($p < 0.025$). According to baseline TEE, 1 pt was grade 0, 4 pts were grade I, 6 pts were grade II, 3 pts were grade III and 2 were grade IV. Two years later 7 pts did not change category, 3 pts showed progression of TAA (1 pt from grade II to grade III and 2 pts from grade III to grade IV), while 6 pts showed regression of TAA (3 pts from grade I to grade 0, 1 pt from grade II to grade 0, 1 pt from II to I and 1 pt from IV to III). Patients who improved were younger (39 ± 14 vs 52 ± 6 yrs, $p < 0.025$) had less severe pretreatment TAA and had a greater LDL decrease (138 ± 56 vs 72.5 ± 54.5 mg/dl, $p < 0.025$), compared with patients who remained stable or deteriorated.

In conclusion, long-term hypolipidemic diet and treatment with pravastatin is effective in producing TAA regression in young hFH pts with moderate atheromatosis. TEE is a valuable method for the evaluation of these changes.

1116-4 Pravastatin Reduces Total Mortality in Patients With Coronary Heart Disease and Average Cholesterol Levels: Relationship of Baseline Cholesterol and Treatment Effects in the LIPID Trial

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Despite benefits of cholesterol lowering treatment seen in earlier trials, treatment effect on mortality in patients with relatively normal cholesterol levels has remained uncertain. The LIPID trial assessed long term effects of pravastatin versus placebo in 9,104 patients with baseline total cholesterol of 4.0-7.0 mmol/L ($155-271$ mg/dl) and a history of acute myocardial infarction (5,754; 64%) or hospitalisation for unstable angina (3,260; 36%). Major treatment outcomes included coronary mortality, total mortality, myocardial infarction, and stroke. The study was also designed to assess treatment effects by baseline lipids and changes in lipids on subsequent outcomes. The study included large numbers with relatively low initial cholesterol levels: 3,793 (42%) with total cholesterol <5.5 mmol/L (213 mg/dl) and 2,678 (30%) with LDL cholesterol <3.5 mmol/L (136 mg/dl).

Interim analysis has shown clear evidence of a reduction in total mortality with pravastatin ($p < 0.003$) and so the LIPID trial is closing early with final analysis to be undertaken after patient visits are completed by September 30, 1997. The relationship between baseline lipid levels and relative reductions in coronary events will be examined as well as the effect of lipid changes on subsequent coronary risk. This large scale trial should enable the relationship of treatment effects with pravastatin and lipids to be estimated much more reliably.

1116-5 Efficacy and Safety of 0.8 mg Dosage of Cerivastatin, a Novel HMG-CoA Reductase Inhibitor

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Cerivastatin (CER) is a novel HMG-CoA reductase inhibitor that reduces cholesterol levels at ultra-low doses. Previous studies up to 0.4 mg produced a log linear dose-response curve with LDL-cholesterol (LDL-C) reductions of 36%.

Purpose: To characterize the efficacy and safety of CER at 0.8 mg/day.

Methods: In this 28 day randomized, double-blind, placebo (PLA)-controlled Phase II trial, 41 patients with primary hypercholesterolemia were stabilized on an AHA Step I diet for 4 weeks prior to randomization to CER 0.8 mg (n = 28) or PLA (n = 13), daily in the evening. LDL-C, total cholesterol (total-C), HDL-C, triglycerides (TRIG) and Lp(a) were measured at weekly intervals. All adverse events were recorded.

Results: Changes in lipid parameters (% from baseline at each post-treatment visit) were as follows:

Parameter	Day 8		Day 15		Day 22		Day 29	
	PLA	CER	PLA	CER	PLA	CER	PLA	CER
LDL-C	5.0	-32.5	4.1	-37.2	3.1	-43.4	1.2	-44.0
Total-C	1.7	-23.9	2.4	-28.3	3.7	-30.1	1	-30.8
HDL-C	2.0	2.0	-1.2	1.0	3.1	2.6	-1.2	3.2
TRIG	-4.3	-14.5	10.2	-18.9	9.6	-9.7	15.9	-11.2

CER significantly reduced total-C, LDL-C and triglyceride levels compared to PLA. Reductions in total-C and LDL-C were apparent after 8 days, and maximal by Day 22. All patients completed the 28-day treatment course. One patient, in the fourth week of treatment with CER, developed pelvic inflammatory disease. No patient exhibited ALT or AST elevations greater than 2 x ULN. One patient, treated with CER exhibited an asymptomatic increase in CK (8 x ULN) on the last day of treatment. This value returned to near normal six days later.

Conclusions: CER 0.8 mg produced an LDL-C reduction of 44% consistent with a continued log linear dose response of 6% additional LDL-C reduction for every doubling of dose. This reduction is comparable with the higher doses of the most effective statins currently marketed.

1116-6 Sitostanol Ester Added to Long-term Simvastatin Treatment of Coronary Patients With Low and High Basal Cholesterol Absorption

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Background: A simvastatin-treated subgroup, not reducing recurrence of major coronary events, was separated from 4S by high basal serum cholestanol and plant sterol and low precursor sterol ratios suggesting that they had high absorption and low synthesis of cholesterol. We assumed that the non-responders might be more responsive to sitostanol ester margarine (SEM)-induced cholesterol malabsorption.

Methods: From a coronary group treated over a year with simvastatin, highest (H; n = 15) and lowest (L; n = 15) absorbers were selected by their basal cholestanol/cholesterol ratio and treated for 3 months with SEM.

Results: Basal total and LDL cholesterol values and their simvastatin-induced reductions were similar in H and L, while the respective cholestanol and plant sterol ratios were 1.6-1.9 times higher in H than L. Addition of SEM further decreased total (-7.6 ± 2.2%) and LDL (-11.7 ± 3.5%) cholesterol in H ($P < 0.01$), while in L the reductions were nonsignificant. Reductions of cholestanol and plant sterol ratios and the increases of precursor sterol ratios were similar in the two groups.

Conclusion: Coronary patients on simvastatin with high baseline cholesterol absorption are benefitted from sitostanol-induced cholesterol malabsorption as compared to those with low absorption and high synthesis. Non-responsiveness to statin may contribute to lacking recurrence of coronary events.

1116-7 Basal Non-cholesterol Sterols Reveal a Subgroup of 4S Not Benefitted by Simvastatin-Induced Decrease of Recurrent Coronary Events

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Background: In Scandinavian Simvastatin Survival Study (4S) simvastatin-induced reduction of coronary events (CE) was not predicted by baseline lipids. The increasing quartiles of the basal cholesterol (C) precursor sterol (IS)/C